UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

CYTYC CORPORATION, Movant, v. DEKA PRODUCTS LIMITED PARTNERSHIP Respondent.	Civil Action No. 05-10932 (WGY)

DECLARATION OF MARC A. COHN IN OPPOSITION TO COUNTER-APPLICATION TO CONFIRM ARBITRATION AWARD

I, Marc A. Cohn, declare as follows:

1. I am currently employed by Howrey LLP in Washington, D.C. I am a member of the Bar of the District of Columbia, and I have actual knowledge of the matter stated in this declaration and could and would so testify thereto.

2. Attached hereto at Exhibit A is a true and correct copy of excerpts from the transcript of the hearing in the arbitration of DEKA Products Limited Partnership ("DEKA") versus Cytyc Corporation ("Cytyc"), American Arbitration Association file No. 11 Y 133 02624 03 (the "Arbitration").

3. Attached hereto at Exhibit B is Exhibit 403 adduced in the Arbitration.

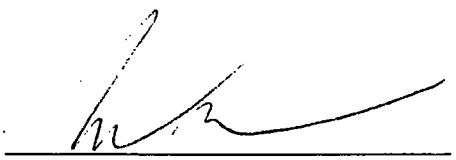
4. Attached hereto at Exhibit C are excerpts of the deposition of Stanley Lapidus in the Arbitration.

5. Attached hereto at Exhibit D are excerpts of the deposition of Dean Kamen in the Arbitration.

6. Attached hereto at Exhibit E are excerpts of the deposition of Robert Goldscheider in the Arbitration.

Signed under penalty of perjury.

Dated: June 2, 2005

By: 

Marc A. Cohn

EXHIBIT A

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AMERICAN ARBITRATION ASSOCIATION

Case No. 11 Y 133 02624 03

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DEKA PRODUCTS LIMITED :
PARTNERSHIP, :
Claimant, :
:
vs. :
:
CYTYC CORPORATION, :
Respondent. :
:
- - - - - - - - - - - - - - - - - - - -x

BEFORE: Hon. E. Leo Milonas, Chairman
Hon. Robert R. Merhige, Jr., Member
Hon. Vincent L. McKusick, Member

PRESENT:

Bromberg & Sunstein LLP
(by Lee Carl Bromberg, Esq., and
Erik Paul Belt, Esq.)
125 Summer Street, Boston, MA 02110-1618,
-and-
DEKA Research & Development Corporation
(by Maureen K. Toohey, Esq.)
340 Commercial Street, Manchester, NH
03101-1129, for the Claimant.

(Continued on Page 2)

Q. Did you agree to assign this patent to Cytyc?

A. Yes, I did.

CHAIRMAN MILONAS: What are you referring to? I missed it.

MR. BROMBERG: Right under the "Inventors" there's the word "Assignee." And it's "Cytyc Corporation."

CHAIRMAN MILONAS: I see. Okay.

Q. Actually, before we get to that, do you see under "Related U.S. Application Data," a little further down, Mr. Kamen, do you see a March 2, 1990 filing date?

A. March 2nd. Yes, I do.

Q. So how did it come about, sir, that you assigned your rights in this patent to Cytyc?

A. Stan called me and said that he was having a problem with his investors. He made a pretty good pitch that, "Dean, this patent is so specifically just for making slides, you have all these other patents on FMS" -- in fact, a lot of them are listed underneath here in these two columns -- and he made it -- he knew our goal and our deal with everybody else was, I own the patents, you get a license. I

again.

A. This seems all encompassing to me. If it's Cytyc Technology, if it's FMS, which is a system that uses solutions and filters, if it's one or the other or both, I get my 1 percent. That's the way I read that.

Q. I don't think there's any dispute, Mr. Kamen, that the provided language means if it falls into either or both of the camps of Cytyc or FMS Technology. My question is, in order for something to be a product disposable, it must both be a filter cylinder or similar disposable and utilize one of those two technologies or both, correct?

A. I believe what you just said is correct.

Q. Is the microscope slide a filter cylinder or similar disposable?

A. Well, it's certainly similar if you're using it to make a slide. If they sold it for some other purpose, it wouldn't be similar. If it's in a pouch with the rest of the stuff to do this job, it's similar.

Q. You were at Mr. Lapidus' deposition, correct?

A. I was there for part of it.

and a fuel filter in front of me, are they similar? Well, they connect to each other and go under the hood of a car. If you put them in front of me and said, Are they similar, they're used to do this particular job, they're each components of what you need to get it done. In that sense, they're similar.

Q. The last sentence of "product disposables" says, "Product disposable presently includes Cytyc's 'TransCyt Filters.'" Do you see that?

A. What page are we on?

Q. "Product disposables," where we've been the whole time.

A. I turned the page. Where are we?

Q. Page D 01582.

A. Product -- I'm sorry?

Q. "'Product disposable presently includes Cytyc's 'TransCyt Filter.'" Do you see that?

A. Yes, I do.

Q. You were aware at the time of the preservative solution, correct?

A. At this time, I was certainly aware you needed preservative solution.

Q. You were aware at the time of the

microscope slide, correct?

A. That you needed a microscope slide to make the system go? Yes.

Q. Did you ever propose that a -- strike that. Did you ever propose language suggesting that that statement said "Product disposable presently includes Cytyc's TransCyt Filters, preservative solution, and microscope slides"?

A. I don't think we had to. It's more -- we didn't say "and the filter and the cap and the label and the bag." The core of the system is what he's referring to when he says "the filter." The statement above it says, if they did it or I did it or both of us. Then it even describes Cytyc Technology, by the way, assuming to be everything under the sun. So it seems to me like we're protected.

Q. Prior to this dispute did you ever expressly state to anyone at Cytyc that they owed you a royalty on the preservative solution?

A. As opposed to just on the disposables?

Q. Expressly referencing preservative solution.

A. I don't think I ever made a request on any

continuations-in-part, reexaminations and reissues of any of the foregoing, and all inventions, drawings, prototypes, schematics, trade secrets, know-how, formulas, compositions of matter" -- composition of matter is everything except energy; it's the known universe -- "designs and intellectual property rights existing that embody or are embodied by, in whole or in part, any of such technology or that pertain to it, including" -- I mean, if that doesn't say, if you make a slide I get my 1 percent, I don't know. I mean, I probably could have found a simpler way to say it.

Q. If we can turn to 5.01, Mr. Kamen.

A. Section 5? Oh, in this, Page 5?

Q. Section 5.01, which also is on Page 5.

A. Yes.

Q. The first clause says, "DEKA has developed the" -- capital P -- "Products." Do you see that?

A. "Has developed the" -- capital P -- "Products," yes.

Q. DEKA didn't develop the preservative solution, correct?

A. No, we didn't.

Q. So the preservative solution can't be a

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AMERICAN ARBITRATION ASSOCIATION

Case No. 11 Y 133 02624 03

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DEKA PRODUCTS LIMITED PARTNERSHIP,
Claimant,

vs.

CYTYC CORPORATION,
Respondent.

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BEFORE: Hon. E. Leo Milonas, Chairman
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(by Maureen K. Toohey, Esq.)
340 Commercial Street, Manchester, NH
03101-1129, for the Claimant.

(Continued on Page 2-2)

THE WITNESS: I don't know of anyone who produces it.

CHAIRMAN MILONAS: Can anyone produce it and sell it? Is it an item which has protection of any kind?

THE WITNESS: The filter, to my knowledge, is not a patented item. If I wanted to produce this and use it, turn it upside down and use it for golf tees, I could do that, and I don't think I would -- no one could prevent me.

CHAIRMAN MILONAS: So if someone chose to manufacture it, they couldn't sell it on the market; is that what you're saying?

THE WITNESS: I think if they wanted to do that as golf tees, they could do that.

CHAIRMAN MILONAS: Not as golf tees but as medical devices.

THE WITNESS: You're probably outside of my scope of expertise.

CHAIRMAN MILONAS: Then you don't know the answer, fine. If you don't know the answer, it's fine.

THE WITNESS: I would think would need some sort of FDA approval to do that.

MR. WOLF: You're absolutely right.

Q. Do you have any independent reason to believe that the ThinPrep Processor as it currently exists practices any DEKA patents?

A. The ThinPrep Processor in operation is, I believe, using the FMS process technology and the Cytyc Technology, which is also included in this agreement and which Mr. Kamen -- to which Mr. Kamen contributed. And the individual disposables are not patented per se, but the individual disposables, when used in concert -- and the only way they're used in concert is using the processor -- that technology must be there. Because that's the justification for the business. That's the justification for people using it and getting a product that works.

Q. I guess I'm going to have to ask a narrower question. Have you done any limitation-by-limitation analyses of any DEKA patents to determine whether Cytyc in any way, with any product, any method, any procedure, infringes any claim?

A. I'm not a patent attorney, and I don't make that kind of a study.

Q. Now, you talked about -- Yvette, if you

EXHIBIT B

US005256571A

United States Patent [19]

Hurley et al.

[11] Patent Number: 5,256,571

[45] Date of Patent: Oct. 26, 1993

[54] CELL PRESERVATIVE SOLUTION

[75] Inventors: Anne A. Hurley, Carver; Daniel C. Lapen, Lancaster, both of Mass.; Peter S. Oud, Bennebroek, Netherlands

[73] Assignee: Cytyc Corporation, Marlboro, Mass.

[21] Appl. No.: 694,452

[22] Filed: May 1, 1991

[51] Int. Cl.[5] G01N 31/00; A01N 1/02

[52] U.S. Cl. 436/17; 436/18; 436/8; 436/826; 435/1; 435/2

[58] Field of Search 435/1, 2, 240.1, 240.2, 435/800; 436/17, 18, 826, 8

[56] References Cited

U.S. PATENT DOCUMENTS

4,090,977	5/1978	Dubin	436/18
4,390,632	6/1983	Carter, II	435/183
4,493,821	1/1985	Harrison	436/18

FOREIGN PATENT DOCUMENTS

0049478	4/1982	European Pat. Off. .
0431385	6/1991	European Pat. Off. .
2099281	12/1982	United Kingdom .

OTHER PUBLICATIONS

WPI, File Supplier, Accession No. 74-81767V (47), Derwent Publications Ltd. London, GB; & JP-A-49 039 437 (Toa Tokushu Denki Co., Ltd) Oct. 25, 1974.

Maitland et al., "Freeze-substitution Staining of Rat Growth Plate Cartilage With Alcian Blue for Electron Microscopic Study of Proteoglycans[1]", *The Journal of Histochemistry and Cytochemistry*, vol. 37, No. 3, pp. 383-387, 1989.

Kurki et al., "Monoclonal antibodies to proliferating cell nuclear antigen (PCNA)/cyclin as probes for proliferating cells by immunofluorescence microscopy and flow cytometry", *Jour. of Immunological Methods*, 109 (1988) pp. 49-59.

Campana et al.,. "Double and triple staining methods for studying the proliferative activity of human B an T lymphoid cells", *Journal of Immunological Methods*, 107 (1988) pp. 79-86.

Ronne, "Chromosome Preparation and High Resolution Banding Techniques. A Review.", Symposium: Cytogenetics and Cell Biology, *J. Dairy Sci.*, 72:1363-1377, (1989).

Levitt et al., "Methanol fixation permits flow cytometric analysis of immunofluorescent stained intracellular antigens", *Journal of Immunological Methods*, 96 (1987) 233-237.

Gill et al., "Laboratory Cytophathology Techniques For Specimen Preparation", The Johns Hopkins Hospital, Sixth Edition, 1980, pp. 3-1-3-3.

Pearson et al., "Evaluation of Collection and Preservation Techniques for Urinary Cytology", Acta Cytologica, 25(3): (May-Jun. 1981), pp. 327-333.

Tsuchihashi et al., "Quantification of Nuclear DNA and Intracellular Glycogen in a Single Cell by Fluorescent Double-Staining", Histochemistry, 63. 311-322 (1979).

Koss, *Diagnostic Cytology and Its Histopathologic Bases*, vol. Two, pp. 1187-1202.

Keebler et al., *A Manual of Cytotechnology*, Sixth Edition, American Society of Clinical Pathologists Press, 1983, pp. 321-322.

Villanueva, A. R., J. Histotechnology, 9(3). 1986. pp. 155-161 (Biosis Abstract).

Rost et al, Histochem. J., 7(4), Jul. 1975, pp. 307-320 (Biosis Abstract).

Baumgaertner et al, J. Clin. Microbiol., 26(10) 1988 pp. 2044-2047 (Biosis Abstract).

Kehr et al, Biologia, 39(11), 1984) p. 1107-1114 (Biosis Abstract).

Primary Examiner—Douglas W. Robinson
Assistant Examiner—Susan M. Weber
Attorney, Agent, or Firm—Lahive & Cockfield

[57] ABSTRACT

An aqueous alcohol buffer solution for substantially ambient, in vitro preservation of mammalian cells for a selected duration. The solution generally contains a water-miscible alcohol in an amount sufficient to fix the sample cells without coagulation, an anti-clumping agent, and a buffer agent to maintain the solution at a pH within a range of four to seven.

15 Claims, No Drawings

CELL PRESERVATIVE SOLUTION

BACKGROUND

This invention relates to a solution and method for preservation of cells at ambient temperatures. The solution and method provide rapid fixation of live cells for subsequent analysis.

It is known in the clinical and research arenas that preservation of cell samples for subsequent analysis is desirable. From a diagnostic standpoint, a specimen is most valuable when it is fresh. The more time that elapses between collection of a specimen and its fixation on a slide or other matrix, the less integrity is retained. Depriving cells of the physiologic conditions of its donor for long periods of time, i.e., minutes, allows autolysis to begin.

In a clinical setting it is often necessary to take samples, e.g., vaginal cells or muscle cells from a patient, which are later stained for histology analysis. Such histochemical staining has unquestionable value in the interpretation and study of cell physiology and pathology, however the staining cannot usually be performed simultaneous with the sampling. It is often-desirable to perform a biopsy on a patient at one time, and to perform cytological or histological analysis of the collected cells or tissue at a different time. Calls often lose integrity in that interim period, thus diminishing the value of the subsequent analysis.

Several types of saline, or balanced salt, solutions are commercially available for preserving cell specimens in the interim between sampling and fixation and/or analysis. A few of these solutions includes Hanks' balanced salt solution, a minimal essential (MEM) tissue culture medium, Polysal ®, and normal saline. The high cost of some medium, such as Hanks' and MEM, prohibits its routine use.

Polysal ®, available from Cutter Biologicals, Emeryville, Calif., is a balanced polyionic electrolyte solution containing sodium chloride, calcium, and magnesium at a physiologically equivalent concentration to normal human plasma. Although an adequate saline solution for relatively short-term storage, it neither inhibits bacterial growth nor enables extended ambient storage.

Hanks' BSS is a modified Ringer solution. It is designed to maintain osmotic pressure within physiologic limits, maintain optimal pH range by including buffer systems, and provides an adequate concentration of inorganic ions for normal cell metabolism. This solution includes a glucose energy source. However, cells lose viability after an exposure of over twenty minutes, which affects cytopathologic analysis.

Many types of clinical tissue and cell samples contain extraneous proteins which interfere with subsequent staining and analysis. Placement of specimen cells in a saline solution does not address some auxiliary problems with such sample integrity. Extended preservation of specimens often results in bacteria growth, which is also nurtured by the balance of prior art normal or augmented saline solutions.

Accordingly, it is an object of the present invention to provide a cell fixing solution and process which preserves cells and tissue for subsequent cytological or histological analysis.

SUMMARY

This invention generally relates to a solution and method for preservation of cells and tissue at ambient temperatures. The solution is an alcohol buffer solution for in vitro preservation of mammalian cells at ambient temperatures following biopsy, and prior to staining or other forms of analysis. In one embodiment, the preservation solution provides a medium for relatively long-term ambient preservation. In another embodiment, the preservation solution provides a medium for transportation and removal of undesired protein from the sample solution.

More specifically, a preservative solution according to the invention has water-miscible alcohol, in combination with an anti-clumping agent and a buffering agent. The alcohol constituent is present in an amount sufficient to fix sample cells or tissue, while the anti-clumping agent is present in an amount sufficient to prevent cells from clumping in solution. The buffering agent is one which maintains the pH of the solution within a range of between about four to about seven for the duration of preservation.

In a preferred embodiment of the invention, the alcohol is one from the group consisting of ethanol and methanol. The anti-clumping agent is a chelating agent, preferably one from the group consisting of ethylenediaminetetra-acetic acid (EDTA), and its salts, such as disodium, tripotassium and tetrasodium. The buffering agent is selected from PBS, Tris buffer sodium acetate, and citric acid. EDTA and its malts may also be used as a buffering agent. In one preferred embodiment, the solution comprises methanol, EDTA, and sodium acetate. In that embodiment, the solution constitutes about 45–55 percent methanol, the EDTA, in the form of glacial acetic acid, constitutes about 2–4 percent, and the sodium acetate buffer constitutes about 6–8 percent.

In another embodiment of the invention, the alcohol is methanol, and the anti-clumping agent is preferably a combination of sodium and potassium EDTA salts, and the buffering agent is an acetate buffer. In one embodiment, the solution comprises methanol, magnesium acetate, calcium acetate, potassium chloride, and sodium chloride. The alcohol constitutes approximately 20 percent of the solution, about 0.1% sodium chloride, 10 mM potassium chloride, 2 mM calcium acetate, and 1 mM magnesium acetate.

In an illustrative practice of the method of the invention, a sample of mammalian cells is provided and, within a predetermined or specified time frame following biopsy, the cells are suspended in a preservation solution of the type described above. In one embodiment of the invention, the suspended cells can be preserved at an ambient temperature in the range of from about 4° to about 38° centigrade (C.) for a period of at least approximately three weeks. Throughout this time, the cells retain sufficient structure to enable staining without a significant loss of integrity.

In another illustrative practice of the method of the invention, a sample of mammalian cells is provided and, within a specified time frame following biopsy, the cells are suspended in a preservation solution of the invention. In that embodiment of the invention, the sample is placed in the preservation solution to remove undesired protein from the cell sample. The clean sample may then be transported in the inventive solution for subsequent analysis and/or storage.

DETAILED DESCRIPTION OF THE INVENTION

The present invention generally relates to an alcohol-buffer solution for the preservation of mammalian cells in suspension at ambient temperature. The solution enhances maintenance of the nuclear structure of the cells, in that it maintains cell membranes intact for subsequent cytological staining. The solution also effectively destroys microbial pathogens in a sample, and inhibits retroviral activity. In one form, the solution removes undesired protein material from the sample.

More particularly, the cell-preservation solution of the invention includes a combination of an alcohol, an anti-clumping agent, and a buffer that maintains the solution at a pH of between about four to seven for the duration of the preservation time.

In one embodiment, the preservation time for cells in the present solutions at ambient temperature (approximately 37° C.), is approximately three weeks. This duration may be altered by both the stored age of the solution prior to ambient cell suspension, the amount of time between cell sampling and cell suspension, and the alcohol content. For example, if the solution has been stored for a significant length of time, in either a refrigerated state or an ambient state, then the remaining cell-preserving viability of the solution may be limited.

In a preferred embodiment, the alcohol is methanol. Other alcohols which may be used include isopropanol and ethanol among others. This alcohol consituent maintains cell DNA integrity and retains the detail of the cell nucleus for subsequent cytological staining and analysis.

In one embodiment of the invention, the alcohol is present in an amount of approximately 45% to 55% by solution. Solutions containing 60% or above of the alcohol constituent tend to exhibit clumping, or coagulation, which interferes with the subsequent ability to affectively stain the sample cells. Conversely, if the concentration of alcohol in this embodiment is at 40% or below, the cells are not sufficiently fixed for relatively long-term preservation, causing the cells to degrade over time. For this embodiment, the solution contains approximately 50% methanol, by solution.

In another embodiment of the invention, the alcohol is present in an amount approximately 20 percent by solution. While this concentration of alcohol, as noted above, does not enable long-term preservation, (i.e., over two days), it does sufficiently fix cells for subsequent analysis. Alternatively, the cells may be transferred from this 20% embodiment solution to a 50% embodiment of the solution, for subsequent long-term preservation prior to analysis.

The inventive solution also contains an anti-clumping agent in an amount sufficient to prevent cell clumping. In one embodiment, the anti-clumping agent is the chelating agent ethylene diamine tetraacetate (EDTA), with the preferred form being the disodium salt. Other chelating agents deemed useful as the anti-clumping agent include cuminin, heparin, streptokinase, and such agents found in lysing or anticoagulant compositions.

The buffer used in the inventive solution has a large buffering range to accommodate for the change in pH resulting from autolytic by-products from the sample cells suspended in the solution. For example, as cervical cells age, they release autolytic by-products that alter the pH balance of the suspension solution. In addition, the preservation of different cell types may require solutions of different acidity and within different pH ranges. Accordingly, a solution having a broad buffering range can be used for a wide range of cell types and is optimal for the solution of the invention. Exemplary cells for which this solution can be used include cervical cells, white blood cells, bronchial cells, and sputum, among others.

Accordingly, a preferred buffer is an acetate buffer, such as sodium acetate, magnesium acetate, calcium acetate, and combinations thereof. While other buffers, such as phosphate or Tris buffers, may be used in the present solution, the effective buffering range of these buffers is deemed to be not as broad at the desired PH as that of acetate.

In addition to being a cell preservative, the inventive solution also kills selected pathogens. For example, in test samples the solution effectively kills the following organisms: *Candida albicans, Aspergillus niger, Escherichia coli, Pseudomonas aeruginosa,* and *Staphylococcus aureus.* This activity is shown in further detail in Example 1 below.

In practicing the method of the invention, a cell sample is obtained from a patient or other cell source. A preservation solution of the type described above is placed either in a vial, on a welled slide, or on an appropriate membrane. The collected cells are then placed in the solution, preferably within one minute following collection. The sooner the collected cells are placed in the preservative solution, the longer the cells can be preserved at ambient temperature suspended in the solution, since the trauma to the cells is minimized.

Following preservation and/or protein removal, when the cells are to be stained or otherwise analyzed, a device can be used to remove suspended cells, along with the suspension preservation medium, and place them on a slide or other appropriate surface for further processing.

The invention is described further in the following non-limiting examples.

EXEMPLIFICATION

EXAMPLE 1

Approximately 20 ml of the preservation solution described above, having the following composition, were aseptically placed in sterile centrifuge tubes, along with an aliquot of one organism to be tested. All samples were plated on Letheen agar. The composition of the preservation solution was:

249 g 180 mM sodium acetate
6 ml 100 mM glacial acetic acid
500 ml methanol
500 ml deionized H_2O

The pH of the resulting solution was adjusted to approximately 5.8. The following organisms were tested for viability, each obtained from the ATCC:

Organism	ATCC No.
Candida albicans	10231
Aspergillus niger	16404
Escherichia coli	8739
Pseudomonas aeruginosa	9027
Staphylococcus aureus	6538

The following test results were obtained:

Organism	Initial Stock Concentration	organisms/ml Time 0	30 Mins.	3 Hrs.
C. albicans	2.9×10^7	<1000	<10	<10
A. niger	5.6×10^7	3.6×10^5	<10	<10
E. coli	2.35×10^7	2.3×10^5	<10	<10
P. aeruginosa	2.0×10^7	<1000	<10	<10
S. aureus	3.0×10^7	1.5×10^5	<10	<10

These results show that the preservative solution of the present invention effectively kills organisms, such as those listed above. In many prior preservative solutions, these organisms frequently multiply in samples, obscuring or interfering with the study of the desired cells. Thus, the solution having the above-identified composition can be used as an antimicrobial solution, in addition to being used as a cell preservative.

EXAMPLE 2

One composition of the preservative solution of the present invention consists of 50% methanol in acetate buffer. The specific formula used in this example, Solution A, is as follows:

3.2 ml glacial acetic acid (CH_3COOH)
7.2 ml 5N NaOH
89.6 ml distilled H_2O
100 ml methanol (MeOH)

A solution of phosophate buffered saline (PBS) in 20% ethanol was used as a control solution, Solution B. A third solution, Solution C, consisted of phosphate buffer, without the saline (NaCl), mixed with the 50% methanol Solution B. The pH of the phosphate buffer solution was initially 7.85. Following the addition of 50 methanol, the pH increased to 9.02. Sodium phosphate monobasic monohydrate (NaH_2PO_4) was added (2.8 g), resulting in a lowered PH of 6.52. The solution was reused to pH 7.5 with 50 methanol.

Cervical cell samples were taken and stored overnight in PBC at 40° C. Samples were pooled, and two 13 ml samples were pipetted into 50 ml centrifuge tubes Samples A and B, respectively), and one 15 ml sample was pipetted into a 50 ml centrifuge tube (Sample C). All three samples were centrifuged for 10 minutes at maximum setting, and the supernatant discarded. Aliquots of Solutions A and B (40 ml each) were added to the remaining pellets of Samples A and B, respectively, while a 50 ml aliquot of Solution C was added to the pellet of Sample C. The following procedure was performed on day zero, then once a week for three weeks, for each sample.

The samples were lightly vortexed to disperse the pellets. Aliquots of 10 ml each were taken from each Sample tube, and placed in a rotor cylinder. The sampes were rotored for 15 seconds at 8V (482 rpm/V). Two slides, having 5 ml of specimen per slide) were prepared and fixed in 95% ethanol for 30 minutes. One of the two slides was immediately stained using routine Pap stain. The second slide was allowed to dry, post-fixation, in a covered dish to be batch stained at the end of the study to reduce stain viability bias.

The following qualitative results were observed:

Soln A	Week	Morphology
4°	0	slight air drying, esp. in inflammatory cells
	1	superior to day 0, esp. inflammatory and epithelial cells
	2	same as week 1
	3	same as week 1; background debris noted
room temp.	0	air drying observed
	1	abnormal cells noted; retains diagnostic features
	2	endocervical cells preserved; same as week 1
	3	same as week 1
37°	0	same as for 4° and room temp specimens, i.e., air drying
	1	rare degeneration in abnormals
	2	abnormal architecture; morphology intact; slight degeneration
	3	same as week 2; endocervical cells noted; background debris noted

Soln B	Week	Morphology
4°	0	some air drying
	1	degeneration noted in inflammatory cells (fuzzy)
	2	good preservation; endocervical cells maintained
	3	inflammatory cells less crisp
room temp	0	air drying
	1	rolling noted
	2	good endocervical cell preservation; increased HK (large gaps); abnormal cells; decrease in cytological detail
	3	endocervical cells preserved; increased epithelial nuclear degeneration
37°	0	air drying
	1	rolling; degeneration in inflammatory cells
	2	degenerated inflammatory cells
	3	degenerated inflammatory cells; some degenerative changes in abnormal cells; rare number of abnormal cells

Soln C	Week	Morphology
4°	0	marked degeneration in inflammatory cells
	1	no inflammatory cell preservation; rare abnormal cells; poor nuclear/cytoplasmic preservation of either normal and abnormal cells
	2	same as for week 1
	3	marked degeneration

These test results demonstrate that optimal results are from Solution A. In that solution, cells remain well-preserved up to three weeks. Some degeneration seen in abnormal cells may be biological in nature.

EXAMPLE 3

The above experiment (Example 2) was performed on cervical specimens known to contain abnormal cells. Such cells included rare squamous atypia (ASM), mild dysplasia (LG), koilacytotic atypia (HPV), and endocervical cells (EC). The results were as follows:

Soln A	Week	Morphology
4°	0	LG; HPV; ASM; reacting EC's
	1	LG; HPV; sheets of EC's
	2	LG; HPV; EC's noted
	3	LG; HPV; sheets of EC's; slight nuclear/cytoplasmic degeneration
room temp	0	
	1	LG; rare HPV, rare koilo, reactin EC's
	2	LG; HPV; reacting EC's
	3	LG; HPV; (metaplastic features); sheets of EC's; Candida noted
37°	0	
	1	LG; HPV (metaplastic features); sheets of EC's; nuclear wrinkling
	2	rare LG; rare HPV; EC's noted

-continued

Soln A	Week	Morphology
	3	LG; HPV; EC's noted

Superior morphology was maintained throughout the study. Abnormal cytologic detail was maintained at all temperatures over the three week period. These results demonstrate that Solution A is optimal for collection and transportation of cell samples.

EXAMPLE 4

A general formula for an alternate embodiment of the preservation solution of the invention is stated as follows:

N/2 liters	deionized H_2O
N × 1.116 g	Na_2 EDTA.$2H_2O$
N × 0.35 ml	glacial acetic acid
(45–55%)	methanol

wherein N represents the final batch solution size. Methanol is added in an amount up to N, within the desired percentage range.

EXAMPLE 5

Another embodiment of the invention includes the following formulation:

1 mM magnesium acetate
2 mM calcium acetate
10 mM potassium chloride
0.1% sodium chloride
20% methanol

In this formulation, the function of the calcium and magnesium ions is the preservation of nuclear morphology of cytologically significant cells. The acetate is present as a buffer that will both stabilize the pH of the solution, and not form precipitates of calcium and magnesium. Such precipitation would happen with a phosphate buffer. The sodium and potassium salts are present to help stabilize the cells and prevent precipitation and coagulation of hemoglobin and other serum proteins. The methanol is present to aid in the lysing of red blood cells, to act as a preservative against bacterial growth, and to help preserve cytologically significant cells.

The invention can be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The present embodiments are therefore to be considered in all respects as illustrative and not restrictive. The scope of the invention is indicated by the appended claims, rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

What is claimed as new and secured by Letters Patent is:

1. An aqueous alcohol-buffer solution for maintaining the structural integrity of mammalian cells in vitro, said solution comprising

A. a water-miscible alcohol in an amount sufficient to fix mammalian cells,

B. an anti-clumping agent in an amount sufficient to prevent the mammalian cells from clumping in said solution, and

C. a buffering agent which maintains said solution, with the mammalian cells, at a pH range of between about two to about seven.

2. The solution of claim 1 wherein said alcohol is selected from the group consisting of ethanol, isopropanol, and methanol.

3. The solution of claim 1 wherein said alcohol is methanol.

4. The solution of claim 1 wherein said anti-clumping agent is a chelating agent selected from the group consisting of ethylenediamine tetraacetic acid and salts thereof.

5. The solution of claim 1 wherein said anti-clumping agent is ethylenediamine tetraacetic acid.

6. The solution of claim 1 wherein said alcohol constitutes about 45 to about 55 percent of said solution.

7. The solution of claim 1 wherein said alcohol constitutes about 50 percent of said solution.

8. The solution of claim 1 wherein said buffering agent is selected from the group consisting of phosphate buffered saline, Tris buffer, sodium acetate, ethylenediamine tetraacetic acid, ethylenediamine tetraacetic acid salts, citric aid and citric acid salts.

9. The solution of claim 1 wherein said buffering agent is sodium acetate.

10. An aqueous alcohol-buffer solution for maintaining the structural integrity of mammalian cells in vitro, said solution comprising, by volume,

A. about forty-five to fifty-five percent methanol,

B. about two to four percent acetic acid, and

C. about six to eight percent sodium acetate buffer.

11. The solution of claim 10 comprising about 50 percent methanol.

12. The solution of claim 10 comprising about three percent acetic acid.

13. The solution of claim 10 comprising about seven percent sodium acetate buffer.

14. The solution of claim 1 wherein said alcohol constitutes about 20 percent of said solution.

15. The solution of claim 1 wherein said anti-clumping agent is an ethylenediamine tetraacetic acid salt selected from the group consisting of sodium and potassium.

* * * * *

EXHIBIT C

Volume I
Pages 1 to 105
Exhibits-See Index

AMERICAN ARBITRATION ASSOCIATION

Case No. 11 Y 133 02624 03

- -x

DEKA PRODUCTS LIMITED PARTNERSHIP,
Claimant,

vs.

CYTYC CORPORATION,
Respondent.

- -x

DEPOSITION OF STANLEY N. LAPIDUS, a witness called on behalf of the Claimant, taken pursuant to Rule 30 of the Federal Rules of Civil Procedure, as well as the applicable provisions of the American Arbitration Association Commercial Rules of Arbitration, before Anne H. Bohan, Registered Diplomate Reporter and Notary Public in and for the Commonwealth of Massachusetts, at the Offices of Helicos BioSciences Corporation, One Kendall Square, Building 200, Cambridge, Massachusetts, on Tuesday, September 7, 2004, commencing at 1:22 p.m.

PRESENT:

Bromberg & Sunstein LLP
(by Erik Paul Belt, Esq.)
125 Summer Street, Boston, MA 02110-1618,
-and-
DEKA Research & Development Corporation
(by Maureen K. Toohey, Esq.)
340 Commercial Street, Manchester, NH 03101-1129, for the Claimant.

(Continued on Page 2)

A. Soon.

Q. Soon. Was this relationship formalized in any sort of document? And let me home in on it. In this time frame.

A. No. To the best of my recollection, the answer is no.

Q. What were the terms of this business relationship, as best you understood it?

MR. SANDERS: I'm sorry, I'm confused as to timing. He said at this time there was no business relationship.

A. There was --

MR. SANDERS: Can you read back the last answer.

(Record read * to **)

Q. So I take it from your answer that at least in beginning of your relationship with Mr. Kamen, you had a verbal agreement?

A. That is correct.

Q. Do you recall the terms of that agreement?

A. Yes.

Q. What were the terms?

A. What we agreed upon was that Dean would undertake the development of prototyping the

technology to be able to suck cells onto a filter, measure the concentration by sucking cells onto a filter. That he would bill me 50 percent of the actual expenses incurred.

I said to Dean, "But I haven't raised any money." And he said, "I'll only send you a bill when you raise the money." And he further put forth a royalty. He said -- I asked, "How much?" He said, "Well, Baxter pays me 3 percent." I said, "Gee, that's a lot."

And then I don't remember the pace of things unfolding, but we wound up at a different spot, including some equity and the royalty.

Q. Let's focus first on the royalty portion of it. Do you recall in this early agreement what the royalty rate agreed upon was?

A. 1 percent.

Q. 1 percent. 1 percent of what? What would the royalty be based on?

MR. SANDERS: Objection.

A. Of the sales attributable to the FMS technology.

Q. How would this FMS technology be -- strike that. Did you discuss how the FMS technology would

be deployed in the system that Dean was prototyping for you?

A. We identified the instrument and the filters.

Q. Let's start with the instrument first. Is this the instrument that became known as the ThinPrep processor?

MR. SANDERS: Objection.

A. Maybe you could rephrase the question.

Q. You said that you had agreed that the royalty would be based on -- strike that. You said the FMS would be deployed in the instrument and the filter, I think.

A. Yes.

Q. Could you describe the instrument for me.

A. The instrument that was developed and eventually marketed is the ThinPrep processor.

Q. What is the filter that you referred to?

A. The plastic cylinder with a membrane, a porous membrane welded to the end.

Q. Do you know whose idea it was to attach a filter membrane to a cylinder?

A. I think it was attach a filter membrane to the cylinder. I think that was actually a guy named

A. I don't recall.

Q. At this point was Cytyc selling the ThinPrep system for use with Pap tests?

A. Only for research -- well, outside the U.S., yes, and in the U.S. for so-called investigational use and research use only.

Q. Cytyc did not have FDA approval at this time for the Pap test?

A. That's correct.

Q. Do you recall when Cytyc obtained FDA approval for the Pap test?

A. In 1996.

Q. This was after you began the company?

A. Yes.

Q. You make a reference here to a "handshake understanding" in the second-to-last sentence. Is that handshake understanding the verbal agreement that you had recounted to me earlier?

A. It is.

Q. Do you recall whether you had any other written agreements leading up to the 1993 License Agreement with DEKA?

A. I do not.

Q. If you'll turn to Page 5 of the License

Q. Do you know what products were sold to be used with the ThinPrep processor?

MR. SANDERS: At that time?

MR. WOLF: At that time, thank you.

A. I don't recall.

Q. Was the filter used?

A. It was.

Q. At that time?

A. It was.

Q. Was the preservative solution sold at that time?

A. It was.

Q. Were there slides sold at that time?

A. I don't recall when we began selling slides.

Q. Are you aware of anything unique about the slides that Cytyc sells with the ThinPrep processor kit?

A. Yes.

Q. What's unique, to your knowledge?

A. The slides have properties which assure that cells stick to the slides.

Q. Do you know when Cytyc first became aware of the potential of making slides with those special

MR. WOLF: Why don't you just put that in the stack.

Q. Whose idea was the special featured slide?

A. My idea.

Q. How did you come up with it?

A. We had two problems. One problem was the cells didn't stick to the slide. Some slides it did; others it didn't. So we figured out what kind of glass worked well.

The other was an issue of assuring a proprietary component. We felt that by putting a trademarked feature on the slide, we would keep others from selling slides that would work on ThinPrep processors. It was a slide with certain electrostatic properties, we made that discovery, and we felt that by putting this special feature on it, we'd be able to protect that as an asset.

Q. Now, when you say "trademark," you're using that loosely. Do you mean trade secret, perhaps?

A. No. I meant that the mark I think is a proprietary mark, that if you made that same mark you would be -- I think -- I don't recall -- I believe there's a ThinPrep logo on the slide.

EXHIBIT D

CONFIDENTIAL, SUBJECT TO PROTECTIVE ORDER

Volume I
Pages 1 to 226
Exhibits 21-25

AMERICAN ARBITRATION ASSOCIATION

Case No. 11 Y 133 02624 03

DEKA PRODUCTS LIMITED PARTNERSHIP,
Claimant,

vs.

CYTYC CORPORATION,
Respondent.

CONFIDENTIAL DEPOSITION OF DEKA PRODUCTS LIMITED PARTNERSHIP, by its designee DEAN KAMEN, and DEAN KAMEN individually, a witness called on behalf of the Respondent, taken pursuant to Rule 30(b)(6) of the Federal Rules of Civil Procedure, as well as the applicable provisions of the American Arbitration Association Commercial Rules of Arbitration, before Anne H. Bohan, Registered Diplomate Reporter and Notary Public in and for the Commonwealth of Massachusetts, at the Offices of Bromberg & Sunstein LLP, 125 Summer Street, Boston, Massachusetts, on Tuesday, September 14, 2004, commencing at 10:00 a.m.

PRESENT:

Bromberg & Sunstein LLP
(by Erik Paul Belt, Esq.)
125 Summer Street, Boston, MA 02110-1618,
-and-
DEKA Research & Development Corporation
(by Maureen K. Toohey, Esq.)
340 Commercial Street, Manchester, NH 03101-1129, for the Claimant.

(Continued on Page 2)

Q. Do you know whether DEKA has any intellectual property rights in the sample collection devices that have been sold by Cytyc?

MR. BELT: Again, the objection to the extent IP calls for a legal conclusion.

MR. WOLF: Understood.

A. Could you define for me what the "sample collection device" is.

Q. Do you know what sample collection devices Cytyc sells currently?

A. I don't know their product line.

Q. Have you heard terms like "Cytobrush" or "spatula" before?

A. Yes.

Q. Does DEKA have any intellectual property rights in the Cytobrush?

A. No.

Q. Does DEKA have any intellectual property rights in the spatula?

A. No.

Q. Have you heard the term used "broom-like collection device"?

A. Yes.

Q. Does DEKA have any intellectual property

rights on the broom-like collection device?

A. No.

Q. We've talked about the slide. Does DEKA have any intellectual property rights in the slide sold by Cytyc?

A. A, I don't know that they sell a slide. B, I don't know whether any of the patents or claims refer to slides. I know we had to put the cells somewhere, so I can't answer that question.

Q. To your knowledge, does DEKA have any intellectual property rights in slide technology?

A. Just slide technology?

Q. Yes.

A. No.

Q. Does DEKA have any intellectual property rights in the vial -- I'm saying vial as opposed to vial with solution -- that Cytyc sells?

A. Again, I don't know that they sell the vial. Again, in the early days of building prototypes, we were trying different shapes for the vial. We were doing different methods of attaching things, figuring out better kinds of lids. I don't know whether that constitutes or resulted in intellectual property.

A. Say the question again.

Q. Did there ever come a time where you changed your position that "Vials filled with collection medium are explicitly excluded from this Agreement"?

A. I'm not sure that I changed my position. The final agreement is different than this agreement. It's not that I changed my position; the agreement changed. The words in the agreement changed.

Q. Is there a single conversation where you recall that you said to Mr. Lapidus, "I expect you will pay royalties on vials filled with collection medium"?

A. No.

Q. Is there a single conversation you recall where Mr. Lapidus said he would be willing to pay royalties on vials filled with collection medium?

A. No.

Q. Do you recall a single document where the parties said, "Royalties will be paid on vials filled with collection medium"?

A. I don't think there's any document that explicitly says that, but I know that the final

EXHIBIT E

AMERICAN ARBITRATION ASSOCIATION

DEKA PRODUCTS
LIMITED PARTNERSHIPS,
Claimant,

Case No.
11 Y 133 02624 03

vs.

CYTYC CORPORATION,

Original Transcript

Respondent.

DEPOSITION
OF
ROBERT GOLDSCHEIDER

16490 Maddalena Place
Delray Beach, Florida

Friday, November 5, 2004
11:15 a.m -- 4:50 p.m.

no one has done what you describe indicates to me that it's something that I as a person who I am would not seek to compete.

Q. And you assume that's because of patent protection issues as opposed to, for example, regulatory requirements, is that correct?

A. Are you referring to FDA when you are talking about regulatory?

Q. Isn't it possible, Mr. Goldscheider, that the reason there is not a competitor on the filter is because of regulatory requirements not patent issues?

A. I'm not certain. I haven't considered the issue.

Q. At a minimum, would you like to amend your report to strike the word patented before the word and proprietary filters?

A. No.

Q. Then I am going to ask you again, what about the filter is patented?

A. It is my understanding that the FMS Technology is important to the operation of the filter and the FMS Technology is the subject of numerous patents in the name of Dean Kamen.

Q. Have you seen a single patent claim that

covers the filter, ever?

A. I have not but I have not looked for them.

Q. So you are willing to say that a filter is patented even though you have never seen a claim that actually covers the filter, is that correct?

A. I suppose so.

Q. Now you say perhaps less innovative elements, referring to the vial, slide and collection device.

Are you aware of the existence of a patent on the collection fluid at issue in this case?

A. I'm aware that a patent exists.

Q. And a patent issues when something is novel, correct?

MR. BELT: You are asking for a legal --

MR. WOLF: He's told us that he is willing to give legal opinions. I don't think --

MR. BELT: I don't think in his expert report he gives legal opinions.

Q. On what ground do you say that the filter is more innovative than the preservative solution?

A. On the basis of Mr. Lapidus who is there. He felt that the FMS Technology, which I believe

Whether or not any others were submitted to it I don't know. But I do believe that I am on safe ground in saying that this solution is not unique, that it is the only one that can perform this task. It seems to work well and that's fine.

Q. What other solution would work?

A. I am not technically qualified to do this but I'm sure that anybody who has the proper chemical background could offer alternatives to it.

Q. So you are just guessing?

A. No, I'm not guessing. I'm basing this on my own experience. There are very few things that are unique in this world.

Q. Is the filter unique in this world?

A. I believe the filter is, but I don't think the other elements are.

Q. What's unique about the filter?

A. It is something which was able to perform something which a skilled and highly talented person like Lapidus could not do, and since that time no improvement has come along that I know of that would obsolete the FMS Technology that's part of the filter.

Q. What FMS Technology is in the filter?

A. Now you are asking me to get into the

technical side of this. I am not somebody who can answer this. I am somebody, however, who can take advice from people I consider to be knowledgeable and negotiate from there.

Q. Who told you that the FMS Technology could be found in the filter?

A. Who told me that the FMS Technology was?

Q. In the filter.

A. Was in the filter?

Q. Yes, that there was FMS Technology embodied in the filter, who told you that?

A. I've seen -- this is the impression I have from reading the documents. Again, I hark back to Lapidus. But I had that impression before I read Lapidus's deposition that this is what was mentioned in the 1989 term sheet.

For instance, it was the thing which Dean had been working on in other contexts which he was able to adapt to this one. It was something of which he has a whole basket full of patents. I've seen a list of them.

I have not seen anything which leads to a contrary conclusion that the FMS Technology did not have any influence in the development of the filter or indeed in the development of the ThinPrep